

Samantha Dye

End of Summer FURSCA Report

My research is focused on synthesizing a light-responsive version of the drug vismodegib, a smoothed inhibitor. Smoothed is a transmembrane protein that is a key component of the Hedgehog signaling pathway. This pathway is very important for tissue proliferation, but when mutations arise, it leads to cancerous cells being formed in the body. The goal of my project is to create a photo-switchable azo analogue of vismodegib that will drastically reduce the harsh side effects of this drug due to the ability of azo-stilbenes to isomerize in response to light. The drug is designed to be taken in its inactive form and activated by photoisomerization in response to light administered selectively to the cancer cells, thus not harming healthy cells in the body.

This summer research period has allowed me to further improve my skills in the lab and learn more about working on synthetic chemistry. I have performed many different types of reactions with varying conditions from 10-minute-long reactions in 100 degree Celsius to overnight reactions left at room temperature. Overall, I have made it about halfway through my synthesis of azo-vismodegib. I have also been working on the synthesis of azo-sonidegib (another Smoothed inhibitor). About halfway through the summer I made it to the last step of my synthesis of azo-sonidegib, however it was not successful. I tried the same reaction a few times with varying conditions, but it became clear that this coupling reaction was not working. With the help of my advisor, Dr. Streu, we came up with a new end to my synthesis that only required me to do 3 more reactions. This is what I am currently working on but will not have time to finish by the end of the FURSCA period.

For future work this fall, I would like to finish the synthesis of both the azo compounds I am working on. In addition, start photophysical characterization of them using UV-Vis to test the ratio of trans to cis and cis to trans transformation upon irradiation of light. I plan to present my research at next year's Elkin Isaac and the American Chemical Society Meeting in Spring 2022. I would like to thank all of those who make FURSCA possible especially the Orpha Leiter Irwin Fellowship who supported my FURSCA research.

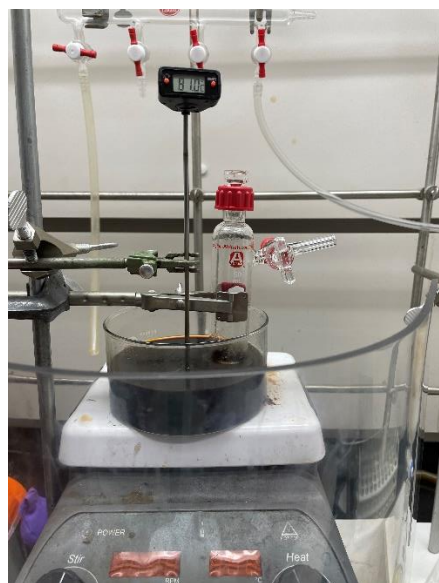
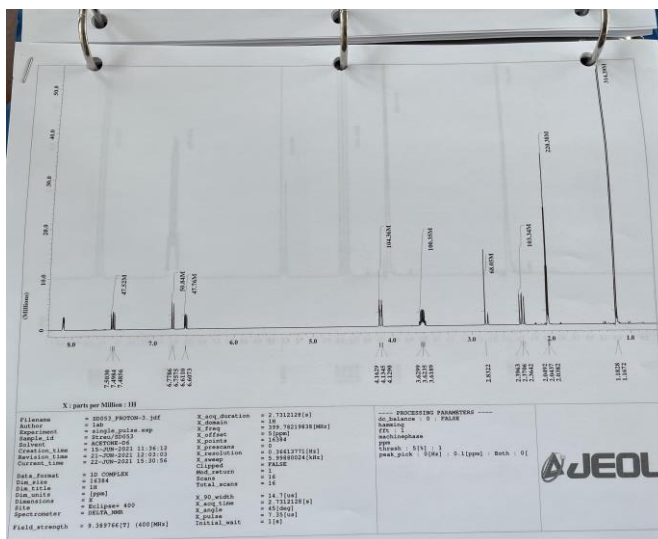


Photo of Buchwald Reaction in Schlenk Tube for the right side of Sonidegib



Graph from Nuclear Magnetic Resonance instrument, which shows peaks corresponding to the Hydrogens in my molecule